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Waiting Time Dynamics in Two-Dimensional Infrared Spectroscopy

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CONSPECTUS

We review recent work on the waiting time dynamics of coherent two-dimensional infrared (2DIR) spectroscopy. This dynamics can reveal chemical and physical processes that take place on the femto- and picosecond time scale, which is faster than the time scale that may be probed by, for example, nuclear magnetic resonance spectroscopy. A large number of chemically relevant processes take place on this time scale. Such processes range from forming and breaking hydrogen bonds and proton transfer to solvent exchange and vibrational population transfer.

In typical 2DIR spectra, multiple processes contribute to the waiting time dynamics and the spectra are often congested. This makes the spectra challenging to interpret, and the aid of theoretical models and simulations is often needed. To be useful, such models need to account for all dynamical processes in the sample simultaneously. The numerical integration of the Schrödinger equation (NISE) method has proven to allow for a very general treatment of the dynamical processes. It accounts for both the motional narrowing resulting from solvent-induced frequency fluctuations and population transfer between coupled vibrations. At the same time, frequency shifts arising from chemical-exchange reactions and changes of the transition dipoles because of either non-Condon effects or molecular reorientation are included in the treatment. This method therefore allows for the disentanglement of all of these processes.

The NISE method has thus far been successfully applied to study chemical-exchange processes. It was demonstrated that 2DIR is not only sensitive to reaction kinetics but also to the more detailed reaction dynamics. NISE has also been applied to the study of population transfer within the amide I band (CO stretch) and between the amide I and amide II bands (CN stretch and NH bend) in polypeptides. From the amide I studies, it was found that the population transfer can be used to enhance cross-peaks that act as structural markers for β-sheet structure in proteins. From the amide I/II investigation, it was found that the amide II band and the hydrogen-bond stretch vibration are important parts of the relaxation pathway for the amide I vibration. With the development of simple approximations, it becomes possible to apply the NISE method even to very big systems, such as the OH stretch of bulk water, which can only be described well when large numbers of coupled vibrations are taken into account.
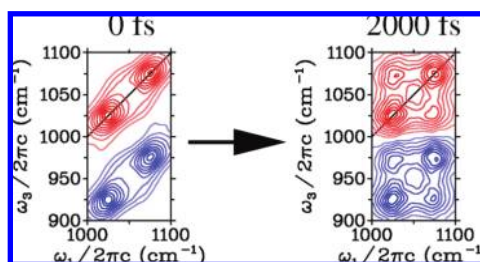
Introduction

Numerous important processes, ranging from electron transfer to hydrogen-bond exchange and molecular reorientation, happen on the ultrafast (femto- and picosecond) time scale. Such molecular-scale processes are important in diverse fields, such as biology, where enzymes perform their function, but also in nano technology, where artificially made molecular motors are developed to perform specific tasks. To understand and possibly control the operation of such systems, one needs to be able to follow the underlying dynamics. A successful example is the molecular-scale flow of electronic excitation energy in biological light-harvesting systems, which has been studied in great detail using pump−probe spectroscopy.[1] However, many interesting systems do not have optical transitions and, therefore, require other

ultrafast spectroscopic techniques to resolve their dynamics. One particularly well-suited method is two-dimensional infrared (2DIR) spectroscopy.[2]

2DIR spectroscopy is a four-wave mixing technique. It involves the excitation of the system with a pump−pulse pair. After a time of free evolution, denoted as the waiting time, the state of the system is read by applying a probe pulse and measuring the emitted signal. The technique is therefore a correlation spectroscopy with similarities to two-dimensional nuclear magnetic resonance (2DNMR).[3] It allows one to follow what happens to the vibrations in a molecule after an initial excitation and provides a two-dimensional spectrum that reveals information on dephasing of the individual vibration and coupling between different vibrations. The latter allows for the determination of structural parameters.[4] However, the real power of 2DIR is its ability to follow femto- and picosecond dynamics in real time by varying the waiting time in the experiment. This allows the tracking of fast chemical exchange,[5,6] vibrational energy transport,[7,8] and orientational dynamics.[9] We refer to this as the waiting time dynamics of the 2DIR spectra.

Experimentally 2DIR spectroscopy has successfully been applied to a wide range of systems.[10] The spectra are, however, often congested and complex to interpret. This calls for a good theoretical method to model the spectra. Of course, such a method should be able to account for all of the dynamics in the system. The simplest simulation methods are completely static and do not allow us to account for any dynamics. In this paper, we will review recent progress in simulating and interpreting two-dimensional infrared spectra with waiting time dynamics. The focus will be on the application of the numerical integration of the Schrödinger equation (NISE) method. The main advantage of NISE over other methods is that it can be used to simulate the spectra even when multiple dynamical processes are entangled. In the following section, the NISE method will be outlined. Next, we will discuss three application areas. Finally, in the Outlook section, we will discuss possible future applications of the method as well as alternatives and improvements of it.

Method

In the NISE method[11−13] for calculating the nonlinear response, the sample is divided into the part that directly interacts with the applied laser fields (denoted the system) and the remaining part that does not (denoted the bath). It is assumed that the system is affected by the applied fields and the bath but that the state of the system does not affect the bath. The system is treated quantum-mechanically, and its evolution can be described by the time-dependent Schrödinger equation

$$\frac{\mathrm{d}\Phi(t)}{\mathrm{d}t} = -\frac{i}{\hbar}H(t)\Phi(t) \tag{1}$$

where the wave function $\Phi(t)$ describes the state of the quantum system and the effective system Hamiltonian $H(t)$ fluctuates because of the perturbations caused by the bath. The time evolution of the bath is then first determined, either by means of Molecular Dynamics (MD) simulations or by using a stochastic model. The state of the bath along the trajectory is used to construct the trajectory of the fluctuating Hamiltonian, where either a model or a first-principles map is used to translate the bath coordinates into an effect on the Hamiltonian. The time-dependent Schrödinger equation cannot be solved directly when the Hamiltonian is time-dependent. Therefore, the trajectory is divided into short intervals during which the Hamiltonian can be taken to be constant.[14] The time evolution during each interval can then be determined by a time evolution matrix given by a simple matrix exponent.

$$U(t + \Delta t, t) \equiv \exp\left(-\frac{i}{\hbar}H(t)\Delta t\right) \tag{2}$$

The time evolution for longer times is found by time-ordered products of the time evolution matrices for the short intervals.

The generic Hamiltonian used to describe 2DIR experiments is of the form

$$H(t) = \sum_i \omega_i(t)B_i^\dagger B_i + \sum_{j\neq i} J_{ij}(t)B_i^\dagger B_j - \sum_i \frac{\Delta_i(t)}{2}B_i^\dagger B_i^\dagger B_i B_i +$$
$$\sum_i \bar{\mu}_i(t)\vec{E}(t)(B_i^\dagger + B_i) \tag{3}$$

Here $B^\dagger$ and B denote, respectively, the Bosonic creation and annihilation operators of vibration i, with frequency ω_i. J_{ij} is the coupling between a pair of vibrations; Δ_i is the anharmonicity of a vibration; and $\bar{\mu}_i$ is the transition dipole vector. The externally applied laser field is $\vec{E}(t)$. The fluctuating frequencies, anharmonicities, and dipoles are typically extracted from MD simulations by using *ab initio* mappings, which relate these quantities to the electrostatic potential or field caused by the environment at the positions of the atoms involved in the vibration. Such mappings already exist for the amide modes of peptides,[15−19] the OH stretch of water,[20] and the CN stretch of nitriles.[21] The long-range couplings J_{ij} are typically given by transition dipole[22] or transition charge[23,24] coupling schemes. For short-range interactions, maps relating the coupling to the Ramachandran angles between amide units in peptides have been constructed using *ab initio* calculations.[22,24,25]
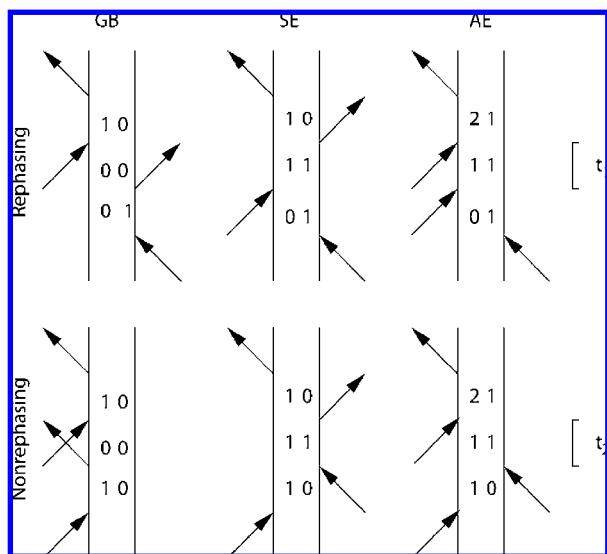
FIGURE 1. Double-sided Feynman diagrams illustrating the six contributions to the 2DIR signal. The arrows indicate the interactions with the laser pulses. The numbers 0, 1, and 2 denote the ground, single excited, and double excited states, respectively. The pairs of numbers indicate the density matrix of the system between the applied pulses. The waiting time is indicated with t_2.

The 2DIR spectrum consists of six types of contributions, namely, the ground-state bleach (GB), the stimulated emission (SE), and the excited-state absorption (EA), each of which has a rephasing and a non-rephasing form. These six contributions are illustrated by their double-sided Feynman diagrams[26,27] in Figure 1. In the GB signal, the first laser pulse brings the system into a coherent superposition of a single excited state and the ground state. The system is brought back to the ground state by the second laser pulse, and during the waiting time (t_2), it is left here. Then, the third pulse again brings the system into a coherent superposition of a single excited state and the ground state, which finally relaxes to the ground state by the emission of the signal. The SE contribution differs from the GB in that the system is left in a single-excited-state population or a coherent superposition between two single-excited states during the waiting time. Finally, the EA is only different from the SE by the fact that the last laser pulse brings the system into a coherence between double- and single-excited states. This last contribution thus involves the double-excited states, making it sensitive to the anharmonicity. If the anharmonicity is zero (i.e., the system is harmonic), the total signal vanishes as a consequence of cancelations between the various contributions.[28]

The simulation of these signal contributions each involves a four-point correlation function of the transition dipoles. Time evolution operators are sandwiched between the transition dipoles to account for the time evolution between the interactions with the laser pulses.[12] The two-dimensional spectra
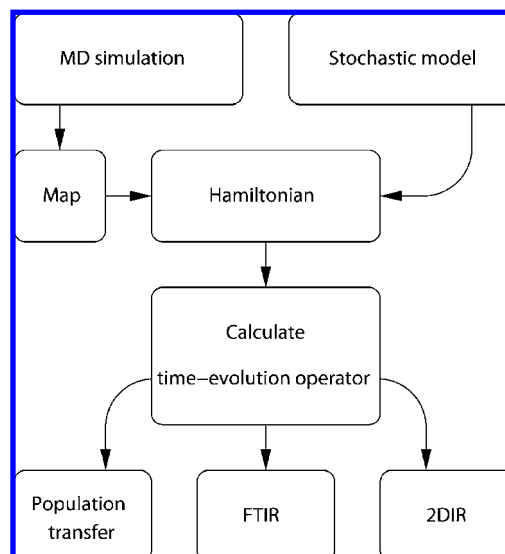
**FIGURE 2.** Flow diagram for the NISE procedure.

are obtained by Fourier transforming the signal with respect to the delay between the first and second pulse as well as Fourier transforming with respect to the time delay between the last pulse and emission of the signal. The frequency associated with the first (second) Fourier transform is denoted $\omega_1(\omega_3)$. For each fixed waiting time t_2, the spectrum may now be plotted as a function of ω_1 (horizontal axis) and ω_3 (vertical axis). The waiting time dynamics is revealed by analyzing the t_2 dependence of the spectra.

A flow chart for the general simulation protocol is given in Figure 2.

Examples of Applications

Chemical Exchange. Chemical reactions are traditionally studied in cases far from equilibrium, with excess of the reactants and following the build up of product molecules under the assumption that the reaction can then be seen as irreversible. Correlation spectroscopies offer the possibility to study chemical reactions as they happen in equilibrium. This has been exploited to measure reaction kinetics and unravel reaction pathways with NMR spectroscopy.[29] While NMR spectroscopy allows us to directly follow reactions on the micro- and nanosecond time scales, 2DIR spectroscopy opens a window to observe femto- and picosecond processes.[6]

For simulation purposes, the NISE method has the advantage over other methods that it can go beyond the approximation of Gaussian fluctuations. This approximation underlies the second-order cumulant-based methods.[30,31] Moreover, NISE allows one to go beyond the Kubo jump models for modeling chemical exchange and, therefore, enables the simulation of exchange dynamics and not merely exchange kinetics.[32] Simulations of model systems can be performed using,
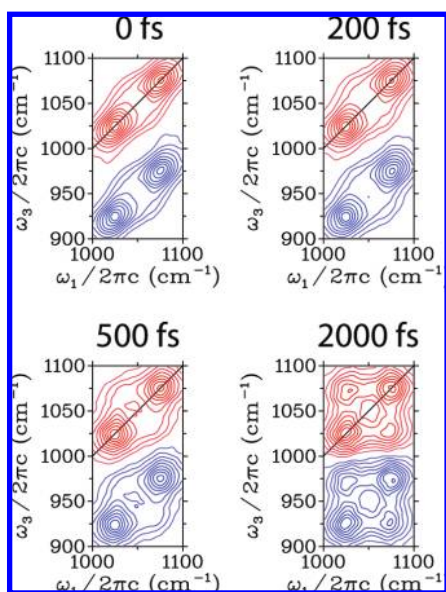
FIGURE 3. 2DIR spectra of chemical exchange in a symmetric double-well potential. The red contour lines indicate bleaching and stimulated emission, and the blue lines indicate excited-state absorption. Reprinted with permission from ref 32. Copyright 2008, American Institute of Physics.

for example, a Langevin equation for the exchange process. This approach was used by us in ref 32 to investigate chemical exchange in a double-well potential.

The Langevin equation for a single reaction coordinate was written

$$m\frac{d^2x}{dt^2} = -\frac{dU(x)}{dx} - m\gamma\frac{dx}{dt} + F^{fluc}(t) \qquad (4)$$

where m is the mass connected with the coordinate x, $U(x)$ is the potential, and γ is the friction constant determining the coupling strength with an external heat bath. F^{fluc} is a random fluctuating force for which Gaussian white noise was used, imposing the correlation function requirement

$$\langle F^{fluc}(t)F^{fluc}(0)\rangle = \delta(t)\gamma mkT \qquad (5)$$

The vibrational frequency of the observed mode was assumed to be proportional to x. The two-dimensional spectrum corresponding to motion in a double-well potential was then simulated.[32] The potential was given by

$$U(x) = \begin{cases} \frac{1}{2}k(x-r)^2, & x \geq 0 \\ \frac{1}{2}k(x+r)^2, & x \leq 0 \end{cases} \qquad (6)$$

The resulting spectra obtained with a suitable set of model parameters[32] are shown in Figure 3. In the used potential, it took about 500 fs to move from one well to the other. This finite reaction time[33] can be observed in the spectra, where

the cross-peaks resulting from the exchange process do not start to grow before this barrier crossing time is reached. While thus far such dynamical delays have not been reported in two-dimensional infrared spectra, they have been observed for electron-transfer processes using optical pump−probe techniques.[34]

For experimentalists, a simple estimate of the expected finite reaction time is useful. In ref 33, rather elaborate estimates are given for different cases. However, a lower limit can be given by using the root-mean-square velocity of a particle with mass M in the gas phase, traveling along the reaction path with length d. The travel time is then $t_B = d\sqrt{(M/3RT)}$, where R is the gas constant and T is the temperature. A reaction barrier and the viscosity of the solvent can only be expected to increase this time. For the chemical-exchange experiment on $Fe(CO)_5$ reported in ref 5, filling in the mass of carbon monooxide and a reaction distance of 3 Å gives an estimated time of 300 fs, well below the detection limit of 1 ps of the experiment. With state-of-the-art 2DIR equipment, having pulse widths below 100 fs, the finite reaction time should, however, be possible to detect in the $Fe(CO)_5$ system. Alternatively, one could use heavier ligands, lower temperature, or a more viscous solvent to increase the finite reaction time.

Population Transfer in Proteins. The amide I band of proteins has received a lot of attention, mostly because this band is intense and the coupling between amide I modes along the protein backbone is strong enough to create collective vibrational modes that depend upon the protein structure. This makes it possible to use 2DIR spectra to distinguish between different secondary structures, such as α helices,[8] β sheets,[35] and 3^{10} helices.[36] The hypothesis of Davydov[37] that energy might be transported efficiently through the amide I modes of, in particular, α helices has sparked studies of the population transfer between amide I modes.[7,38]

In ref 39, the NISE method was applied by us to simulate the population transfer between amide I modes in a β hairpin, trpzip2, in aqueous solution. In the hairpin, two dominant excitonic bands exist in the amide I region. These are denoted (a^-)s and (a^+)s.[40] The simulations showed vibrational population transfer between these two states on a 500 fs time scale (Figure 4). In the 2DIR spectrum, this results in the growth of the cross-peaks between these two states and a decay of the diagonal peaks upon increasing the waiting time (see Figure 5). The cross-peaks between the (a^-)s and (a^+)s states are used as structural markers for β-sheet structure,[35] and it was therefore proposed by us that increasing the waiting time can be used to enhance such structural markers.
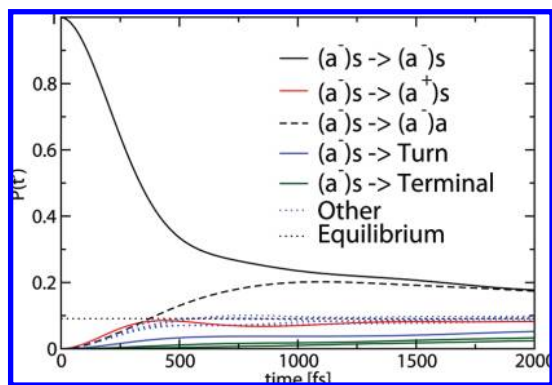
FIGURE 4. Population of different symmetry states in trpzip2 after an initial excitation of the (a⁻)s state. Reprinted with permission from ref 39. Copyright 2008, Biophysical Society.
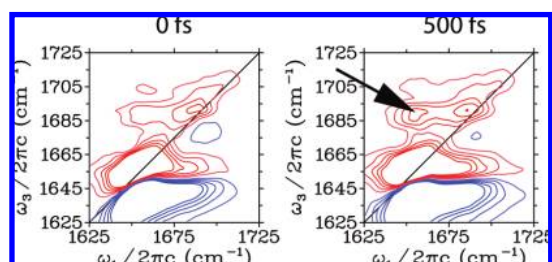
FIGURE 5. 2DIR spectra of trpzip2 at different waiting times. The arrow highlights one of the cross-peaks growing because of population transfer between the vibrational states. Contour lines are drawn as in Figure 3. Reprinted with permission from ref 39. Copyright 2008, Biophysical Society.

The states in the amide I band turn out to have a relatively short vibrational lifetime of the order of 1 ps.[2,41] Such a short lifetime is of course unfavorable for energy transport. It has been suggested that the reason for the short lifetime is efficient population transfer to other modes, such as the amide II band and interpeptide hydrogen-bond vibrations.[7,41−44] The NISE method was applied[19] to the *N*-methyl acetamide (NMA-d) molecule solvated in D_2O, treating both the amide I and amide II vibrations quantum-mechanically and other coordinates, such as the hydrogen-bond vibrations, classically. It was found that the hydrogen-bond fluctuations facilitate an efficient population transfer between the amide I and amide II modes. A population transfer time from amide I to amide II of 790 fs was found, and it was demonstrated that this can be extracted from the relative intensity between cross-peaks and diagonal peaks in the 2DIR spectrum (see Figure 6).[19] This suggests that the dominant relaxation pathway of the amide I mode in solution occurs via the amide II mode and the hydrogen-bond vibration for which the oxygen atom is an acceptor. Others have suggested alternative relaxation pathways,[43−45] which cannot be completely excluded from the above simulation. However, clear experimental evidence
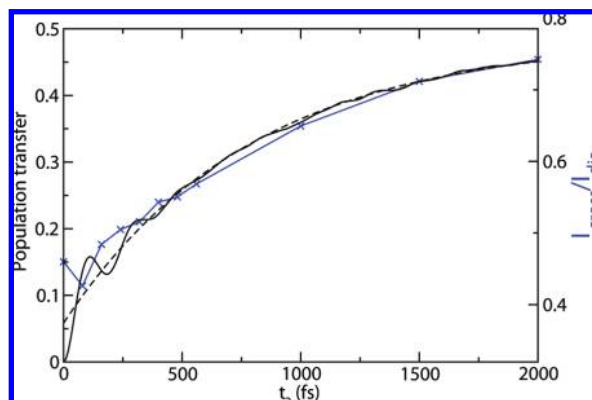
FIGURE 6. Population transfer between amide I and amide II in *N*-methyl acetamide in D_2O. The calculated population in the amide II mode after an initial excitation of the amide I mode (solid black line, left *y* axis) is compared to the relative cross-peak intensity (blue line, right *y* axis). The population transfer was fitted with an exponential function with a 790 fs time constant (dashed black line, left *y* axis) Reprinted with permission from ref 19. Copyright 2008, American Institute of Physics.

exists for the presence of the amide I to amide II transfer, while other pathways have thus far not been observed.[41]

Bulk Water and Large Systems. Pump−probe experiments demonstrated that the anisotropy of the OH stretch vibration in bulk water decays on a sub 200 fs time scale because of exciton transport between different water molecules.[46] Simulation of the exciton transfer in water confirmed this interpretation.[47] In more recent 2DIR experiments,[48] the spectral diffusion resulting from the exciton transfer was observed as well. The simulation of the 2DIR spectrum of bulk water is particularly challenging because of the large number of coupled oscillators that one needs to treat. This is in particular a problem for the propagation of the double-excited states involved in the excited-state absorption signal. The number of these states grows as $N \times (N + 1)/2$, where N is the number of oscillators. By introducing an approximation that splits the propagation of the double-excited states into a harmonic and an anharmonic term, Paarman and co-workers, however, successfully applied the NISE method to simulate the 2DIR spectra at different waiting times.[49,50] They used the trick that the propagation of the harmonic term is trivial, when propagation of the singly excited states is known and the anharmonic part of the Hamiltonian is rather sparse. The time evolution of the double-excited states can then be found with the Trotter formula.[49,50] It should be emphasized that this is an approximation, where the error term is proportional to the commutator between the harmonic and anharmonic parts of the Hamiltonian and the square of the small time interval. The error can, thus, be reduced by using small time intervals. By employing this approximation, the NISE method should also

be applicable to the calculation of 2DIR spectra of other extended systems, such as proteins, DNA, and other macroscopic systems of biological relevance.

Outlook

As demonstrated above, the NISE approach allows for the simulation of spectra involving very general dynamical processes in a wide variety of systems. The approach, however, still has a few limitations that pose a challenge for the development of better simulation methods in the future. The fundamental approximation that NISE relies upon is the fact that the bath is not affected by the excitation of the vibrations, which allows for the molecular dynamics to be performed independently of the spectral simulation. In reality, the bath degrees of coordinates are of course influenced by the vibrational excitation. The neglect of this effect has several consequences, where the most significant is the lack of thermalization in the NISE simulation. If one waits long enough, all levels will be equally populated and not obtain the population predicted by the Boltzman factor.

Approaches that allow for correct thermalization include the time-dependent self-consistent field method,[51] where bath and system degrees are simulated simultaneously, including the feedback to the bath, and stochastic Schrödinger and Liouville equations[52] based on the influence functional formalism.[53] These more elaborate methods are, of course, also more time-consuming and challenging to apply to large systems.

In all of the discussed examples, the necessary parameters for the fluctuating Hamiltonian were known. For small systems, it should be possible to combine the NISE method with a minimization algorithm to fit a few unknown parameters.

Despite the above-mentioned minor drawback of the NISE method, it is very well-suited for simulating 2DIR spectra of dynamical systems. It requires no *a priori* knowledge of what motion is important for the spectral waiting time dependence and no assumption that the dynamics is Gaussian. The method can be applied to extended systems, ranging from large peptides and small proteins to bulk water.

BIOGRAPHICAL INFORMATION

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REFERENCES

1 van Amerongen, H.; Valkunas, L.; van Grondelle, R. *Photosynthetic Excitons*; World Scientific: Singapore, 2000.

2 Hamm, P.; Lim, M. H.; Hochstrasser, R. M. Structure of the amide I band of peptides measured by femtosecond nonlinear-infrared spectroscopy. *J. Phys. Chem. B* **1998**, *102*, 6123–6138.

3 Hahn, E. L. Spin echoes. *Phys. Rev.* **1950**, *80*, 580–594.

4 Golonzka, O.; Khalil, M.; Demirdöven, N.; Tokmakoff, A. Coupling and orientation between anharmonic vibrations characterized with two-dimensional infrared vibrational echo spectroscopy. *J. Chem. Phys.* **2001**, *115*, 10814–10828.

5 Cahoon, J. F.; Sawyer, K. R.; Schlegel, J. P.; Harris, C. B. Determining transition-state geometries in liquids using 2D-IR. *Science* **2008**, *319*, 1820–1823.

6 Woutersen, S.; Mu, Y.; Stock, G.; Hamm, P. Hydrogen-bond lifetime measured by time-resolved 2D-IR spectroscopy: *N*-Methylacetamide in methanol. *Chem. Phys.* **2001**, *266*, 137–147.

7 Backus, E. H. G.; Nguyen, P. H.; Botan, V.; Pfister, R.; Moretto, A.; Crisma, M.; Toniolo, C.; Stock, G.; Hamm, P. Energy transport in peptide helices: A comparison between high- and low-energy excitations. *J. Phys. Chem. B* **2008**, *112*, 9091–9099.

8 Woutersen, S.; Hamm, P. Time-resolved two-dimensional vibrational spectroscopy of a short α helix in water. *J. Chem. Phys.* **2001**, *115*, 7737–7743.

9 DeCamp, M. F.; DeFlores, L.; McCracken, J. M.; Tokmakoff, A.; Kwac, K.; Cho, M. Amide I vibrational dynamics of *N*-methylacetamide in polar solvents: The role of electrostatic interactions. *J. Phys. Chem. B* **2005**, *109*, 11016–11026.

10 Cho, M. Coherent two-dimensional optical spectroscopy. *Chem. Rev.* **2008**, *108*, 1331–1418.

11 Torii, H. Time-domain calculations of the polarized Raman and two-dimensional infrared spectra of liquid *N,N*-dimethylformamide. *Chem. Phys. Lett.* **2005**, *414*, 417–422.

12 Jansen, T. I. C.; Knoester, J. Nonadiabatic effects in the two-dimensional infrared spectra of peptides: Alanine dipeptide. *J. Phys. Chem. B* **2006**, *110*, 22910–22916.

13 Jansen, T. I. C.; Zhuang, W.; Mukamel, S. Stochastic Liouville equation simulation of multidimensional vibrational line shapes of trialanine. *J. Chem. Phys.* **2004**, *121*, 10577–10598.

14 Leforestier, C.; Bisseling, R. H.; Cerjan, C.; Feit, M. D.; Friesner, R.; Guldberg, A.; Hammerich, A.; Jolicard, G.; Karrlein, W.; Meyer, H. D.; Lipkin, N.; Roncero, O.; Kosloff, R. A comparison of different propagation schemes for the time-dependent Schrodinger equation. *J. Comput. Phys.* **1991**, *94* (1), 59–80.

15 Hayashi, T.; Zhuang, W.; Mukamel, S. Electrostatic DFT map for the complete vibrational amide band of NMA. *J. Phys. Chem. A* **2005**, *109*, 9747–9759.

16 Ham, S.; Cho, M. Amide I modes in the *N*-methylacetamide dimer and glycine dipeptide analog: Diagonal force constants. *J. Chem. Phys.* **2003**, *118* (15), 6915–6922.

17 Schmidt, J. R.; Corcelli, S. A.; Skinner, J. L. Ultrafast vibrational spectroscopy of water and aqueous *N*-methylacetamide: Comparison of different electronic structure/molecular dynamics approaches. *J. Chem. Phys.* **2004**, *121*, 8887.

18 Jansen, T. I. C.; Knoester, J. A transferable electrostatic map for solvation effects on amide I vibrations and its application to linear and two-dimensional spectroscopy. *J. Chem. Phys.* **2006**, *124*, 044502.

19 Bloem, R.; Dijkstra, A. G.; Jansen, T. I. C.; Knoester, J. Simulation of vibrational energy transfer in two-dimensional infrared spectroscopy of amide I and amide II modes in solution. *J. Chem. Phys.* **2008**, *129*, 055101.

20 Auer, B. M.; Skinner, J. L. IR and Raman spectra of liquid water: Theory and interpretation. *J. Chem. Phys.* **2008**, *128*, 224511.

21 Choi, J. H.; Oh, K.-I.; Lee, H.; Cho, M. Nitrile and thiocyanate IR probes: Quantum chemistry calculation studies and multivariate least-square fitting analysis. *J. Chem. Phys.* **2008**, *128*, 134506.

22 Torii, H.; Tasumi, M. Ab initio molecular orbital study of the amide I vibrational interactions between the peptide groups in di- and tripeptides and considerations on the conformation of the extended helix. *J. Raman Spectrosc*. **1998**, *29* (1), 81–86.

23 Hamm, P.; Woutersen, S. Coupling of the amide I modes of the glycine dipeptide. *Bull. Chem. Soc. Jpn*. **2002**, *75*, 985–988.

24 Jansen, T. I. C.; Dijkstra, A. G.; Watson, T. M.; Hirst, J. D.; Knoester, J. Modeling the amide I bands of small peptides. *J. Chem. Phys*. **2006**, *125*, 044312.

25 Gorbunov, R. D.; Stock, G. Ab initio based building block model of amide I vibrations in peptides. *Chem. Phys. Lett*. **2007**, *437*, 272–276.

26 Mukamel, S. *Principles of Nonlinear Optical Spectroscopy*; Oxford University Press: New York, 1995.

27 Mukamel, S. Multidimensional fentosecond correlation spectroscopies of electronic and vibrational excitations. *Annu. Rev. Phys. Chem*. **2000**, *51*, 691–729.

28 Tanimura, Y.; Mukamel, S. Two-dimensional femtosecond vibrational spectroscopy of liquids. *J. Chem. Phys*. **1993**, *99*, 9496–9511.

29 Perrin, C. L.; Dwyer, T. J. Application of two-dimensional NMR to kinetics of chemical exchange. *Chem. Rev*. **1990**, *90*, 935–967.

30 Kubo, R. Generalized cumulant expansion method. *J. Phys. Soc. Jpn*. **1962**, *17* (7), 1100–1120.

31 Mukamel, S. Nonimpact unified theory of four-wave mixing and two-photon processes. *Phys. Rev. A: At., Mol., Opt. Phys*. **1983**, *28*, 3480–3492.

32 Jansen, T. I. C.; Knoester, J. Calculation of two-dimensional infrared spectra of ultrafast chemical exchange with numerical Langevin simulations. *J. Chem. Phys*. **2007**, *127*, 234502.

33 Zhang, B. W.; Jasnow, D.; Zuckerman, D. M. Transit-event durations in one-dimensional activated processes. *J. Chem. Phys*. **2007**, *126*, 074504.

34 Hannappel, T.; Burfeindt, B.; Storck, W.; Willig, F. Measurement of ultrafast photoinduced electron transfer from chemically anchored Ru—dye molecules into empty electronic states in a colloidal anatase TiO_2 film. *J. Phys. Chem. B* **1997**, *101*, 6799–6802.

35 Demirdöven, N.; Cheatum, C. M.; Chung, H. S.; Khalil, M.; Knoester, J.; Tokmakoff, A. Two-dimensional infrared spectroscopy of antiparallel β-sheet secondary structure. *J. Am. Chem. Soc*. **2004**, *126* (25), 7981–7990.

36 Maekawa, H.; Toniolo, C.; Moretto, A.; Broxterman, Q. B.; Ge, N.-H. Different spectral signatures of octapeptide 3_{10}- and α-helices revealed by two-dimensional infrared spectroscopy. *J. Phys. Chem. B* **2006**, *110*, 5835–5837.

37 Davydov, A. S. *Solitons in Molecular Systems*; Reidel: Dordrecht, The Netherlands, 1985.

38 Botan, V.; Backus, E. H. G.; Pfister, R.; Moretto, A.; Crisma, M.; Toniolo, C.; Nguyen, P. H.; Stock, G.; Hamm, P. Energy transport in peptide helices. *Proc. Natl. Acad. Sci. U.S.A*. **2007**, *104*, 12749–12754.

39 Jansen, T. I. C.; Knoester, J. Two-dimensional infrared population transfer spectroscopy for enhancing structural markers of proteins. *Biophys. J*. **2008**, *94*, 1818–1825.

40 Dijkstra, A. G.; Knoester, J. Collective oscillations and the linear and two-dimensional infrared spectra of inhomogeneous β-sheets. *J. Phys. Chem. B* **2005**, *109*, 9787–9798.

41 DeFlores, L.; Ganim, Z.; Ackley, S. F.; Chung, H. S.; Tokmakoff, A. The anharmonic vibrational and relaxation pathways of the amide I and amide II modes of *N*-methylacetamide. *J. Phys. Chem. B* **2006**, *110*, 18973–18980.

42 Dijkstra, A. G.; Jansen, T. I. C.; Bloem, R.; Knoester, J. Vibrational relaxation in simulated two-dimensional infrared spectra of two amide modes in solution. *J. Chem. Phys*. **2007**, *127*, 194505.

43 Fujisaki, H.; Yagi, K.; Hirao, K.; Straub, J. E. Quantum dynamics of *N*-methylacetamide studied by the vibrational configuration interaction method. *Chem. Phys. Lett*. **2007**, *443*, 6–11.

44 Nguyen, P. H.; Stock, G. Nonequilibrium molecular-dynamics study of the vibrational relaxation of peptides in water. *J. Chem. Phys*. **2003**, *119*, 11350–11358.

45 Rubtsov, I. V.; Hochstrasser, R. M. Vibrational dynamics, mode coupling, and structural constraints for acetylproline—NH_2. *J. Phys. Chem. B* **2002**, *106* (35), 9165–9171.

46 Woutersen, S.; Bakker, H. J. Resonant intermolecular transfer of vibrational energy in liquid water. *Nature* **1999**, *402*, 507–509.

47 Torii, H. Time-domain calculations of the polarized raman spectra, the transient infrared absorption anisotropy, and the extend of delocalization of the OH stretching mode of liquid water. *J. Phys. Chem. A* **2006**, *110*, 9469–9477.

48 Kraemer, D.; Cowan, M. L.; Paarmann, A.; Huse, N.; Nibbering, E. T. J.; Elsaesser, T.; Miller, R. J. D. Temperature dependence of the two-dimensional infrared spectrum of liquid H_2O. *Proc. Natl. Acad. Sci. U.S.A*. **2008**, *105*, 437–442.

49 Paarmann, A.; Hayashi, T.; Mukamel, S.; Miller, R. J. D. Probing intermolecular couplings in liquid water with two-dimensional infrared spectroscopy. *J. Chem. Phys*. **2008**, *128*, 191103.

50 Paarmann, A.; Hayashi, T.; Mukamel, S.; Miller, R. J. D. Nonlinear vibrational response of coupled anharmonic system—Towards the 2DIR spectrums of H_2O; Laubereau, A., Mantel, K.-H., Zinth, W., Eds.; TRVS XIII Conference, Freising, Germany, 2007; p 19.

51 May, V.; Kühn, O. *Charge and Energy Transfer Dynamics in Molecular Systems*; Wiley-VCH: Berlin, Germany, 2000.

52 Stockburger, J. T.; Grabert, H. Exact c-number representation of non-Markovian quantum dissipation. *Phys. Rev. Lett*. **2002**, *88*, 170407.

53 Ishizaki, A.; Tanimura, Y. Nonperturbative non-Markovian quantum master equation: Validity and limitation to calculate nonlinear response functions. *Chem. Phys*. **2008**, *347*, 185–193.